The claims presented above incorporate changes as indicated by the marked-up versions below.

1. (**Amended**) A method for potentiating morphogen activity, comprising administering to a mammal a composition comprising a molecule that overcomes ~~capable of releasing~~ morphogen inhibition.

2. (**Amended**) A method for promoting neuronal cell growth, comprising administering to a mammal a composition comprising a molecule that overcomes ~~capable of releasing~~ morphogen inhibition, thereby to potentiate growth-promoting effects of endogenous morphogens.

3. (**Amended**) A method for treating a disorder characterized by neuronal cell loss, comprising administering to a mammal a composition comprising a molecule that overcomes ~~capable of releasing~~ morphogen inhibition, thereby to potentiate growth-promoting effects of endogenous morphogens.

4. (**Amended**) A method for treating a neurodegenerative disorder, comprising administering to a mammal a composition comprising a molecule that overcomes ~~capable of releasing~~ morphogen inhibition.

8. (**Amended**) The method of claim 3 or 4, wherein said disorder is ~~selected from the group consisting of:~~ Alzheimer's disease, Parkinson's disease, Huntington's disease, senile dementia, alcohol-induced dementia, ~~and~~ or stroke.

9. (**Amended**) The method of claim 1, 2, 3 or 4, wherein said agent that overcomes ~~capable of releasing~~ morphogen inhibition is ~~selected from the group consisting of~~ a cytokine antagonist, a retinoid antagonist, ~~and~~ or a protein kinase A inhibitor.

11. (**Amended**) The method of claim 10, wherein said neuropoetic cytokine antagonist is ~~selected from the group consisting of~~ an LIF antagonist ~~and~~ or a CTNF antagonist.

12. (**Amended**) The method of claim 11, wherein said LIF antagonist is a ~~monoclonel~~ monoclonal antibody to the gp130 protein.

15. (**Amended**) The method of claim 9, wherein said protein ~~kinese~~ kinase A inhibitor is ~~selected from the group consisting of~~ (2-p-~~bromocynnamylaminoethyl~~ bromocinnamylaminoethyl)-isoquinolinesulfonamide, an enantiomer of dibutyryl cAMP, or ~~and~~ an enantiomer of cAMP.

16. (**Amended**) The method of claim 7, wherein said morphogen comprises an amino acid sequence selected from ~~the group consisting of~~ a sequence: (a) having at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, residues 330-431 of SEQ ID NO: 2; (b) having greater than 60% amino acid sequence identity with said C-terminal seven-cysteine skeleton of human OP-1; (c) defined by Generic Sequence 7, SEQ ID NO: 4; (d) defined by Generic Sequence 8, SEQ ID NO: 5; (e) defined by Generic Sequence 9, SEQ ID NO: 6; (f) defined by Generic Sequence 10, SEQ ID NO: 7; ~~and~~ or (g) defined by OPX, SEQ ID NO: 3.

17. (**Amended**) The method of claim 7, wherein said morphogen is ~~selected from the group consisting of~~ human OP-1, mouse OP-1, human OP-2, mouse OP-2, 60A, GDF-1, BNT2A, BMT2B, DPP, Vgl, Vgr-1, BNW3, BNW5, ~~and~~ or BW6.

19. (**Amended**) The method of claim 1, wherein the ~~A method for potentiating morphogen activity comprising the step of administering to a mammal a composition comprising a~~ molecule ~~that~~ binds an endogenous ligand for ~~a receptor selected from the group consisting of~~ a cytokine receptor ~~and~~ or a retinoid receptor.

21. (**Amended**) The method of claim 20, wherein said neuropoetic cytokine receptor is ~~selected from the group consisting of~~ an LIF receptor ~~and~~ or a CTNF receptor.

24. (**Amended**) The method of claim 1, wherein the molecule is ~~A method for potentiating morphogen activity comprising the step of administering to a mammal a composition comprising~~ a cAMP-dependent messenger pathway inhibitor.

25. (**Amended**) The ~~mehted~~ method of claim 24, wherein said cAMP-dependent messenger pathway inhibitor comprises a protein kinase A inhibitor.

26. (**Amended**) The method of claim 25, wherein said protein ~~kinese~~ kinase A inhibitor is ~~selected from the group consisting of~~ (2-p-~~bromocynnamylaminoethyl~~ bromocinnamylaminoethyl)-isoquinolinesulfonamide, an enantiomer of dibutyryl cAMP, or ~~and~~ an enantiomer of cAMP.

27. (**Amended**) A screening method for identifying a molecule that potentiates ~~capable of potentiating~~ morphogen activity, comprising ~~the steps of~~ (1) providing a test cell comprising a morphogen inhibitory element, wherein said test cell, when contacted with OP-1, does not undergo~~ing~~ tissue morphogenesis; (2) exposing said test cell to OP-1 and a candidate molecule; and (3) identifying a molecule that potentiates ~~capable of potentiating~~ morphogen activity as a candidate that overcomes ~~releases~~ morphogen inhibition ~~permiting~~ and permits said test cell to undergo OP-1-induced tissue morphogenesis.

28. (**Amended**) The screening method of claim 27, wherein said test cell is obtained ~~selected~~ from: ~~the group consisting of~~ sympathetic nerves, hippocampus, cerebral cortex, striatum, kidney, liver, adrenals, urinary bladder, ~~and~~ or testes.

Applicants have amended claims 1-4, 8, 9, 11, 12, 15-17, 19, 21, and 24-28, to correct typographical or grammatical errors and to enhance their clarity. Applicants submit that there is no narrowing of scope in any respect due to these amendments.

In reply to the outstanding Restriction Requirement, mailed Dec. 18, 2001, in connection with the above application, Applicants hereby elect Group I (claims 1-18) with traverse, for the reasons which follow. The time period for response has been extended to April 18, 2002, by the accompanying petition for a three-month extension of time.

The Examiner contends that the inventions of Groups I-IV do not relate to a single general inventive concept since they lack the same or corresponding special technical features. Moreover, the Examiner also contends that Groups I-IV lack unity of invention because the PCT Rules do not provide for the search and examination of more than one claimed method.

Applicants respectfully submit that all four groups relate to a single general inventive concept, i.e., potentiation of morphogen activity by overcoming morphogen inhibition. Group I-III claims are all directed to methods of potentiating morphogen activities by releasing morphogen inhibition, using various kinds of specific agents / steps. For example, as amended, the only former Group II independent claim (claim 19) and the only former Group III independent claim (claim 24) now both depend on Group I independent claim 1. Thus, Applicants submit that all these claims relate to a single novel inventive concept.

In addition, Applicants submit that Group IV claims, which are directed to methods to screen for agents / molecules that potentiates morphogen activity, also relate to the same inventive concept.

The Office Action asserts that the invention listed as Groups I-IV do not relate to a single general inventive concept because they lack the same or corresponding special technical features. Specifically, the Office Action contends that the technical feature of Group I claims is administering a composition comprising a molecule capable of releasing morphogen inhibition, which feature is not required for the remaining Groups. Applicants respectfully disagree.

As argued above, the technical feature behind all these Groups, especially Groups I-III, is potentiation of morphogen activity by releasing morphogen inhibition. Former Groups I-III simply achieves this common technical feature through different means, such as releasing morphogen inhibition (by cytokines, RAs, cAMP stimulating molecules, etc.) using different agents (such as cytokine inhibitors / antagonists, RA receptor inhibitors / antagonists, PKA inhibitor, etc.). In fact, searching of Group I claims necessarily searches claims belonging to former Groups II and III (see claim 10 of Group I and claim 20 of Group II; also see claim 15 of Group I and claim 26 of Group III). Applicants respectfully submit that the inventions of Groups I, II and III can be efficiently searched and examined together, and that the relevant art for each group can be found in the same classes (or closely related classes) as the art for the other group. In this respect, Applicants note that there is no indication that the appropriate classes and subclasses for each group are different. Applicants submit that resources, both on the part of Applicants and the Examiner, can be used most efficiently by examining these groups together.

Thus, at least Groups I-III claims meet the unity of invention requirement of PCT Rule 13.1. Accordingly, in view of the foregoing, Applicants respectfully request that the restriction requirement, at least with respect to Groups I, II and III, be withdrawn.

The Examiner has also imposed an election of species requirement with respect to certain species of the above-identified invention. These species include the following: a species of agents capable of releasing morphogen activity, a species of retinoid antagonist/receptors, a species of protein kinase A inhibitors, a species of morphogen amino acid sequences, a species of morphogens, a species of disorders, and a species of test cells. The Examiner has further stated that Applicants must elect a single species to which the claims shall be restricted if no generic claim is finally held allowable, and claims readable on the elected species.

Applicants have elected, with traverse, Group I claims (claims 1-18). Consequently, Applicants also hereby elect, with traverse, and for search purposes only, the following species: 1) a cytokine antagonist (the agent of releasing morphogen activity group); 2) RA receptor antagonist (one species from the retinoid antagonist / receptor group); 3) H89 / (2-p-bromocinnamylaminoethyl)-5-isoquinolinesulfonamide (one species from the PKA inhibitor group); 4) SEQ ID NO: 2 (one species from the morphogen amino acid sequence group); 5) OP-1 (one species from the morphogen group); and 6) Alzheimer's disease (one species from the disorder group).

Furthermore, if the Examiner finds the above argument persuasive and withdraws the restriction requirement between Groups I-III, Applicants further elect, with traverse and for search purposes only, the following species if Group II is rejoined with Group I: RA receptor antagonist (one species from the retinoid antagonist / receptor group). Applicants further elect, with traverse and for search purposes only, the following species if Group III is rejoined with Group I: H89 / (2-p-bromocinnamylaminoethyl)-5-isoquinolinesulfonamide (one species from the PKA inhibitor group). Applicants further elect, with traverse and for search purposes only, the following species if Group IV is rejoined with Group I: sympathetic nerves (one species from the test cell group).

These species are elected for search / examination purposes only. Claims readable on the elected species regarding Group I include claims 1-12, and 16-18. Claims readable on the elected

species regarding Group II include claims 19 and 22. Claims readable on the elected species regarding Group III include claims 24-26. Claims readable on the elected species regarding Group IV include claims 27-32.

As to the Group I species election requirement 1), and 3) - 6), (as well as all Groups II-IV species elections), Applicants submit that species subjected to election are encompassed by Markush groups. Pursuant to MPEP 803.02, "If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions." Applicants submit that such is the case in claims 8, 9, 15, 16, 17, and 26. In addition, Applicants respectfully point out that the search of the Markush-type claim will be extended to non-elected species should no prior art be found that anticipates or renders obvious the elected species (MPEP 803.02).

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

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